REMARKS

On January 28, 2004, the above-referenced application was filed with 32 claims. The claimed application is generally directed to organ and tissue augmentation that utilizes two populations of cells with distinct functions, a first population of cells that is transiently transfected to express an angiogenesis modulating agent, and a second population of cells to be assimilated at the target site.

Restriction Requirement

On January 27, 2005, a restriction requirement was issued. The restriction requirement required election of one of two inventions, claims drawn to a method of organ augmentation or claims drawn to a method of tissue repair. Via a telephone conversation with the Examiner, Applicants provisionally elected claims drawn to a method of organ augmentation with traverse. No further election was required. Original claims 1-13 and 23-29, drawn to a method of organ augmentation, were fully examined. Included in the original claims were claims 1 and 3-7, shown below.

1. A method of organ augmentation comprising the steps of:
   transfecting a population of cells with a plasmid encoding an angiogenesis modulating agent; and
   implanting the transfected cells into a target tissue region where the cells will express the angiogenesis modulating agent thereby inducing assimilation and differentiation of cells in the target region.

3. The method of claim 1, wherein the population of cells comprises undifferentiated cells.

4. The method of claim 1, wherein the population of cells comprises vascular endothelial cells (EC).

5. The method of claim 1, wherein the method further comprises co-administering a second population of cells.

6. The method of claim 5, wherein the second population of cells comprises undifferentiated cells.

7. The method of claim 5, wherein the second population of cells comprises vascular endothelial cells (EC).

On January 4, 2010, Applicants presented claim amendments to narrow the population of vascular endothelial cells in claim 7 to a population of endothelial progenitor cells, as well as new claims that recite the first or second population of cells comprises endothelial progenitor cells, claims 38, 39 and 42.

Subsequently, in the next Office Action dated March 30, 2010, the Examiner withdrew claims 7, 38, 39 and 42 as reciting endothelial progenitor cells. The Examiner stated that claims 7, 38, 39 and 42 were drawn to non-elected subject matter since "the populations of vascular endothelial cells and myoblasts have been constructively elected by original presentation for prosecution on the merits."

However, there is no basis for the Examiner's assertion that "the species of vascular endothelial cells and myoblasts have been *constructively elected* by original presentation for prosecution on the merits." In fact, the original claims, including claim 5 (as shown above), recited "co-administering a second population of cells" – without restriction to vascular endothelial cells or myoblasts. Moreover, claim 6 (which was the subject of four prior Office Actions) further defined the second population of cells to comprise "*undifferentiated cells.*" Both of these claims encompass endothelial progenitor cells – and neither claim was the subject of a restriction requirement during the six-year pendency of this application. Hence, the Examiner's assertion of *constructive election* by the applicant is plainly incorrect.

Additionally, claim 7 originally recited that the second population comprises *vascular endothelial cells*. The amendment to which the Examiner objects would simply *narrow* this claim to *endothelial progenitor cells*. Applicant's specification clearly defines vascular endothelial cells as *including* endothelial progenitor cells. See, for example, paragraph [0120]:

> In another aspect of the present invention, tissue neovascularization can be enhanced using transient expression of VEGF and ***vascular endothelial cells (EC)*** within the tissue that incorporate into blood capillaries. ***Various types of EC including***, but not limited to, . . . ***progenitor EC*** . . . ***can be used*** for angiogenesis and vasculogenesis.

(Emphasis added.) See also, paragraph [0124]. Thus, the amendment to claim 7 does not switch species at all but rather simply narrows the claim. The same reasoning also applies to new claims 38-39 and 42.

Pursuant to 37 C.F.R §1.111(b), on June 30, 2010, Applicants duly requested reconsideration of the restriction requirement. An Advisory Action dated July 15, 2010, maintained the restriction requirement.

In the Advisory Action dated July 15, 2010, the Examiner argues that the population of cells was originally claimed as undifferentiated cells (claim 3), vascular endothelial cells (claim 4) or myoblasts (claim 12) and the co-population was originally claimed as undifferentiated cells (claim 6), vascular endothelial cells (claim 7) or myoblasts (claim 27). As the Examiner considers both endothelial progenitor cells and myoblasts species to be undifferentiated cells, presentation of both endothelial progenitor cells and myoblasts in the original claims would have resulted in restriction. However, the invention, as originally claimed and as it currently stands, claims a population of cells (first population) and a co-population of cells (second population). A restriction requirement to a single species of undifferentiated cells would have been improper, and remains improper, as both the first and second populations of cells can comprise separate populations of undifferentiated cells.

The Examiner further argued that endothelial progenitor cells cannot be accurately called a type of vascular endothelial cells. However, the claims need to be construed in light of the specification. As described in the specification in paragraph [0120], and reprised here, vascular endothelial cells (also called EC) are defined as:

> including, but are not limited to, human umbilical vein EC (HUVEC), human dermal microvascular EC (HDMEC), bovine aortic EC (BAEC), bovine capillary EC (BCE), ***progenitor EC***, and $CD34^+$ mononuclear cells.

Therefore, the Examiner's conclusion that vascular endothelial cells are mature cells, distinct from undifferentiated progenitor endothelial cells is inconsistent with the teachings of the Applicant's specification.

Therefore, for at least the reasons set forth above, the restriction requirement should be withdrawn, and claims 7, 38-39 and 42 should be examined on their merits.

Premature Final Rejection

Applicants' invention is directed to a method of organ augmentation by co-administration of two populations of cells with different functions. Independent claim 1 is directed to a method of organ augmentation using the two populations of cultured cells, the first population transiently transfected to express VEGF and the second population to assimulate at the target region, *implanted together in an injectable polymer matrix* to induce assimilation and differentiation at the target region. Independent claim 23 is directed to a method that involves implanting a first population of cultured cells transiently transfected with a plasmid expressing an angiogenesis modulating agent with at least a second population of cells *cultured on a matrix* to produce an organ construct such that the angiogenesis modulating agent induces the second population of cells to assimilate and differentiate at the target site.

The Examiner correctly noted that this claim was recently broadened by amendment. In a response submitted on January 4, 2010, independent claims 1 and 23 were amended to remove a step of "encapsulating the transfected first population of cells." The removed cell encapsulation step was reintroduced in dependent claims 10 and 33. No amendments were made to change the scope of the recited *matrix element* in any of the claims.

On March 30, 2010, the Examiner issued a "Final" Office action rejecting claims 1-4, 6, 12, 23, 25, 26, 28, 40, 41 and 43 as obvious under a substantially new ground for rejection, the combination of Badylak et al., U.S. Patent Application Pub. No. 2003/0216811 ("Badylak"), Badylak et al., Biomaterials, 1999, and Penn et al., U.S. Patent Application Pub. No. 2004/01611412. The Examiner apparently argued that a sheet of small intestinal submucosa

(SIS) of Badylak is the same as the polymeric matrix (or matrix material) of Applicant's claims. However, nothing in Applicant's amendment changed the scope of the recited *matrix element* in any of the claims. The citation of the Badylak references (as disclosures of matrix materials) as a new ground for rejection under MPEP 706.07(a) precluded the issuance of a final rejection.

Pursuant to 37 C.F.R §1.111(b), on June 30, 2010, Applicants duly requested reconsideration of the "finality" of the Examiner's grounds for rejection. An Advisory Action mailed on July 15, 2010, maintained the finality. The Examiner stated that the scope of the claims was significantly changed (broadened) and in considering the claims in their amended state, the new ground of rejection was necessary. However, the Badylak reference was purportedly applied by the Examiner because of the disclosure of "*submuscosa tissue-derived grafts and methods of using said grafts to repair damaged or diseased tissue*." There is no basis for the Examiner's assertion on page 24 of the Office Action dated March 30, 2010 that "Applicant's amendment *necessitated* the new ground(s) for rejection."

As no amendments were introduced to alter that matrix material and the new rejections over Badylak were applied as purporting to teach the same *matrix material*, Applicants' amendments could not have *necessitated* the new ground(s) for rejection. Applicants respectfully request the withdrawal of the finality and that prosecution be reopened.

CONCLUSION

For all the reasons above reconsideration and withdrawal of the restriction requirement and the premature "final" rejection as maintained in the Advisory Action dated July 15, 2010 are requested.

Please inform us aware of your decisions on the two issues presented in this petition at your earliest convenience. If you believe that a telephone call would facilitate the resolution of any outstanding issues, please do not hesitate to contact the undersigned. Thank you for your assistance in this matter.

The Director is hereby authorized to charge any deficiency in the fees filed with this paper, asserted to be filed with this paper or which should have been filed with this paper (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 141449, under Order No. 105447-2.

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